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Better Fighting Through Chemistry?The Role of FDA Regulation in Crafting the Warrior of the Future

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Food and Drug Law: Final Paper

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Abstract

This paper examines how FDA might respond to attempts by the U.S. military to offer troops an experimental, performance-enhancing drug or medical device to improve alertness, prevent fatigue, and obviate the basic human need for sleep. This paper chronicles military performance enhancement throughout human history, identifies future approaches to military performance enhancement currently being pursued by the American military, and examines the historical relationship between FDA and the military. Based on this historical and policy background, this paper argues that the unique regulatory concerns raised by experimental military performance enhancement technologies will create new strains on the relationship between FDA and the American military.

Introduction

Imagine an American military populated by soldiers who never need to sleep, always stay alert, and never feel fatigued. Special operations forces that can march 100 miles non-stop. Aviators who see the sun rise and set multiple times between each takeoff and landing. Submarine days that last 80 hours rather than 18. This scenario seems impossible at first glance, a futurist fantasy along the lines of teleportation devices, time travel and mental telepathy. However, the American military is not only imagining but is currently developing drugs and medical devices that may make the ‘sleepless soldier’ a reality in the near future. The recent controversies over ‘go-pills’ and the use of experimental bio-defense drugs have demonstrated that FDA already faces a formidable task in regulating military applications of potentially dangerous drugs. However, the new crop of experimental performance enhancement technologies likely will present even greater difficulties for FDA when and if the Department of Defense decides to use or test them on troops in the field.

This paper will attempt to answer a somewhat ominous question: How might FDA respond to attempts by the U.S. military to offer troops an experimental, performance-enhancing drug or medical device to improve alertness, prevent fatigue, and obviate the basic human need for sleep? This paper will approach this question from the points of view of history, regulation, public policy and ethics. Part One sets out the history of military performance enhancement, from the age of the Vikings through modern times. Part Two will examine projects currently being sponsored by the American military that are seeking to develop new technologies to boost troop performance in the field. Part Three describes the regulatory and political dimensions of the relationship between FDA and the military since the Second World War. Part Four analyzes the regulatory concerns raised by experimental drugs with military applications, keeping in mind FDA's current capabilities and limitations.

I.

The History of Military Performance Enhancement

Throughout human history, societies have sought to gain every possible advantage over their adversaries in battle. Tactics, manpower, position on the battlefield and weaponry are the most obvious means of achieving superiority in war. However, there are also numerous instances in which civilizations have employed psychoactive drugs to enhance the alertness, stamina and bravery of their warriors.

A. Military Use of Drugs Other Than Amphetamines

The amphetamine-based ‘go-pills’ currently offered to American troops are only one of a panoply of pharmacological compounds that have been used to boost performance in battle. The Germanic sagas and other source materials from Northern Europe in the Middle Ages speak of a particularly fearless (and particularly feared) class of warriors known as ‘berserks’ or ‘berserkers’:

‘They advanced without mail-coats, and were as frenzied as dogs or wolves; they bit their shields; they were as strong as bears or boars; they struck men down, but neither fire nor steel could mark them. This was called the Berserk Rage.’¹

Their apparent superhuman strength and intimidating demeanor made berserkers extremely valuable to Scandinavian kings bent on achieving military superiority over their neighbors:

According to [a poet at Harald Fairhair’s court], Harald’s court included a company of picked fighters on whom he particularly relied—the berserks, also known as ‘wolf-skins’. From many attests it appears that there was an aura of mystery and horror surrounding such men...²

Until relatively recently, the true source of the ‘berserk rage’ remained mysterious. However, modern scholars have posited a persuasive theory connecting the berserk rage to the ingestion of the *amanita muscaria* mushroom, commonly known as the fly agaric.³

The fly agaric grows wildly throughout Siberia and Northern Europe and has been used as a socially-acceptable intoxicant by indigenous peoples throughout the region since time immemorial. When consumed by humans, this species of mushroom has a pronounced stimulant effect:

³See Siri Melchior, *On Going Berserk* (June 5, 1967) (unpublished manuscript, on file with the Economic Botany Library of Oakes Ames, Harvard Botanical Museum).

A small dose (or the initial effect of a larger one) causes bodily stimulation and a desire for movement and physical exercise. Under its influence a Koryak man is reported to have carried a 120 lb (some 53 kg) sack of flour a distance of ten miles, something he would not have been able to do normally.⁴

The strength and enthusiasm that the drug encourages would have been highly desirable attributes in a warrior engaged in hand-to-hand combat, especially if he were facing a sober enemy. It is perhaps not surprising, therefore, that the mushroom's use by soldiers in the region even extended into the early 19th century:

During a march of the Varmland troops in 1814, a Swedish officer noticed that some of his men were under an attack of wild raging and that they were foaming at the mouth. An investigation disclosed that these soldiers had eaten fly agaric to put themselves in a good fighting mood.⁵

While we will likely never know for certain whether the berserk rage was truly brought on by fly agaric mushrooms, the evidence for the connection is quite persuasive. The mushrooms grow wild in regions that were once inhabited by the Vikings, they saw widespread civilian use throughout the region, and the effects of the drug bear an uncanny resemblance to extant accounts of berserker behavior.

While the berserkers present the most striking historical example of performance enhancing drugs employed in a military context, the general practice was far more widespread, both geographically and pharmacologically. Thus, in his account of a journey to Constantinople in 1610, the English poet George Sandys observed: 'The Turkes are also incredible takers of Opium...carrying it about them both in peace and in warre; which they say expelleth all feare, and maketh them courageous...'”⁶ While opium has been used generally as a painkiller, Sandys' account suggests that Turkish warriors actually ingested the drug *before* battle rather than afterwards. While the stimulant effects of the fly agaric no doubt provided a greater enhancement

⁶Richard Davenport-Hines, *THE PURSUIT OF OBLIVION: A GLOBAL HISTORY OF NARCOTICS 1500-2000*, at 12 (2001).

to warriors' prowess in battle, the military value of having such a 'fearless' and 'courageous' fighting force should not be underestimated.

The coca plant, indigenous to South America and familiar to pre-Columbian civilizations, particularly the Incas, provides another example of military performance enhancement. When chewed, the leaves of the coca plant act as a stimulant: "[coca] alkaloids act directly on the central nervous system to alleviate hunger, thirst and fatigue. . . ."⁷ Chewing coca seems to have been as commonplace among the Inca as tobacco use is in contemporary Western society—its ingestion was not restricted to religious or recreational contexts.⁸ Although it is difficult to establish for certain that Inca warriors actually chewed coca in battle, it would not require a great logical leap to assume so. It has been observed that "[t]he Spanish invaders [exploited the] stimulating effects [of coca] to increase the work capacity of their Inca slaves, whom they forced to mine gold."⁹ The Conquistadors certainly had some basis for their realization that the plant provided a valuable means of improving the productivity of the Incas whom they had conquered. Assuming the Conquistadors learned of the stimulant effects of coca by observing Incas using the drug in their everyday lives, it is more likely than not that its usage had extended into the military context in the pre-Columbian period.

Finally, the unexpurgated lyrics of the well-known Mexican folksong, *La Cucaracha*, which was originally a Zapatista marching song, attests to the use of marijuana among Mexican soldiers during the Mexican Revolution:

La cucaracha, la cucaracha	<i>The cockroach, the cockroach</i>
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⁷*Id.* at 138.

⁸*See id.*

⁹*Id.* at 138.

Ya no puede caminar; *Can no longer walk,*
 porque no tiene, porque le falta *Because he hasn't, because he hasn't*
 Marihuana que fumar. *Marijuana to smoke.*¹⁰

Zapatista soldiers were referred to in the Mexican slang of the time as “cockroaches.” This stanza suggests that the Zapatista soldiers smoked marijuana to combat fatigue on long marches. These four examples, from widely disparate times and places, demonstrate that military performance enhancement through chemistry is not a new or novel idea.

B. Amphetamines in Combat

Amphetamine (betaphenylisopropylamine) was first identified in 1910 and was first synthesized and marketed as a decongestant under the trade name Benzedrine in 1932.¹¹ However, there is evidence suggesting that *ma huang*, an herb containing the stimulant ephedrine—which has been known in Chinese medicine for centuries and was the subject of recent controversy for its use as a dietary supplement in the United States—may have been used by soldiers to keep them awake while performing night watch duties along the Great Wall.¹² In Western countries, amphetamines—particularly Dexedrine (dextramphetamine sulfate)—have been used to combat fatigue among soldiers since the middle of the 20th century.¹³ During the Second World War, after

¹⁰ See Frances Toor, A TREASURY OF MEXICAN FOLKWAYS 310, 413-14 (DATE).

¹¹ See Davenport-Hines, *supra* note 6, at 241.

¹² See Richard Martin, *It's Wake-Up Time*, WIRED, Nov. 2003 [available at: www.wired.com/wired/archive/11.11/sleep_pr.html]; see also Arthur C. Gibson, *Ma Huang: An Ancient Chinese Stimulant* in *Writeups and illustrations of economically important plants* [available at: <http://www.botgard.ucla.edu/html/botanytextbooks/economicbotany/Ephedra/>]

¹³ Performance Maintenance During Continuous Flight Operations: A Guide for Flight Surgeons (NAVMED P-6410), Naval Strike and Air Warfare Center, Jan. 1, 2000, at 8; see also GlaxoSmithkline, *Prescribing Information for Dexedrine* [available at: us.gsk.com/products/assets/us_dexedrine.pdf].

a German pilot who had been shot down was found to be carrying amphetamine tablets, the British Royal Air Force began issuing the drug to its own pilots. By the end of the war, British troops—including aviators, sailors and infantrymen—had been issued a total of 72 million amphetamine tablets, while American troops consumed even greater quantities of the drug.¹⁴ Consumption of amphetamines by American soldiers nearly doubled during the Vietnam War.¹⁵ As will be discussed in greater detail, *infra*, today Dexedrine tablets, euphemistically referred to as ‘go pills,’ are still made available to American combat pilots and, most likely, to special operations forces, as well.¹⁶

Until 1957, the sanctioned use of amphetamines by American and European soldiers fit squarely into the long, worldwide tradition of military performance enhancement outlined, *supra*. The Vikings’ fly agaric, the Incas’ coca, the Turks’ opium and the Mexicans’ marijuana were all generally accepted for use by the civilian population in the societies that produced these enhanced warriors. Similarly, during the first decades of amphetamine production, there was little stigma attached to its use. It was neither unusual nor untoward for world leaders, respected intellectuals and suburban housewives alike to take amphetamines on a regular basis.¹⁷

However, dramatic changes in social mores and government regulation of drugs during the late 1950s distinguish the more recent use of amphetamines by the military from its historical precursors. In 1957, troubled by the increasing recreational use and abuse of amphetamines, the Federal Bureau of Narcotics classified amphetamines as Schedule II controlled substances, meaning that this class of drugs had a high potential

¹⁴See Davenport-Hines, *supra* note 6, at 241.

¹⁵See *id.*

¹⁶See Brad Knickerbocker, *Military Looks to Drugs for Battle Readiness*, THE CHRISTIAN SCIENCE MONITOR 1 (Aug. 9, 2002).

¹⁷See Davenport-Hines at 242-45.

for addiction, although it also had legitimate medical uses.¹⁸ This classification placed restrictions on the distribution and prescription of amphetamines and contributed to a general sense of social stigma except where it was used to fulfill a legitimate therapeutic purpose.¹⁹

Even before 1957, the military use of amphetamines in America and Europe can be distinguished from earlier instances of pharmacological performance enhancement. In general, it seems that warriors who took drugs to bolster their fighting capabilities did so of their own volition, without any centralized military authority endorsing or requiring their use. For example, the berserkers were a small class of warriors who likely fought alongside entirely sober compatriots—berserk rage was not a requirement for service. There is even evidence that, although Viking rulers considered berserkers a valuable military tool, their continual ingestion of fly agaric mushrooms—both in peacetime and in war—was sometimes seen as a nuisance.²⁰ This love/hate relationship between berserkers and their lieges suggests that the use of fly agaric was not required and that sometimes public policy actually counseled against encouraging its use, notwithstanding its strategic value. The accounts of the use of drugs by Incan, Turkish and Mexican forces similarly evidence that soldiers were not commanded by their superiors to use drugs in battle: individual warriors simply did so as a matter of course on the basis of a wholly personal decision.

While the issue of required use of stimulants will be examined, *infra*, in the context of informed consent, as a general matter amphetamine use was the product of centralized military policy. During the Second World War, the French, German and American militaries all provided amphetamine tablets to their respective troops—whether they wanted them or not. British aviators during the war felt a certain level of discomfort with the new performance enhancing drug they were being given:

¹⁸See Davenport-Hines, *supra* note 6, at 246; *see also Controlled Substances Act*, 21 U.S.C.S. § 812 (1996).

¹⁹See 21 U.S.C.S. § 821.

²⁰See Simpson, *supra* note 1, at 153.

‘Pilots as a class,’ reported an RAF medical officer, ‘did not like being doped, and there was a rather well-marked feeling in the Air Force against improvements in performance being obtained by what seemed to the men to be rather “phoney” [sic] means.’²¹

This resistance may have been more a product of flyboy machismo than wariness about the effects of the chemical compound itself. Nevertheless, the important point is that, even though RAF pilots felt uneasy about “being doped” and may have preferred to test their skills while sober, they likely ingested a significant number of the 72 million Dexedrine tablets consumed by British forces during the war. Some other motivating factor must have been at work, with top-down institutional pressure to take the drugs being the most likely candidate. Similarly, while modern American aviators are not required to take ‘go pills,’ they likely feel significant pressure to do so by merit of the fact that the drugs are being supplied by superiors under the rubric of general military policy, rather than their being used in a more decentralized fashion, with individual soldiers acquiring the drugs from sources outside the military, as has been the usual pattern for drug use among warriors throughout human history.

II.

The Role of DARPA in Developing New Means of Military Performance Enhancement

The history of military performance enhancement will not end with amphetamines. The Defense Advanced Research Projects Agency (DARPA), the Defense Department agency primarily responsible for cutting-edge military research, is currently exploring new technologies, pharmacological and otherwise, to keep soldiers awake and alert.

In response to the 1958 launch of Sputnik by the Soviet Union, Congress authorized the Secretary of Defense

to develop a regime for conducting basic and applied research in the field of military technology.²² DARPA, then known as the Advanced Research Projects Agency (ARPA), was designed to operate independently of the three branches of the Armed Services.²³ Today, DARPA still enjoys “substantial autonomy and freedom from bureaucratic impediments.”²⁴ According to Department of Defense Directive 5134.10, which implements the Congressional mandate by establishing guidelines for DARPA, the Director of the agency reports directly to the Undersecretary of Defense for Acquisition Technology Logistics, with the Director of Defense Research and Engineering serving as DARPA’s “Principal Staff Assistant.”²⁵ DARPA’s mission is to “serve as the central research and development organization of the Department of Defense with a primary responsibility to maintain U.S. technological superiority over potential adversaries.”²⁶ DARPA is a relatively small agency with an operating budget in FY2003 of \$2.6 billion.²⁷ Not surprisingly, therefore, instead of conducting its own internal research projects, DARPA personnel perform a pure oversight function, awarding research funding to outside contractors in industry and academia.²⁸ Although DARPA does consider the potential commercialization of research for civilian use, its primary function is “conducting long-range, high-risk research and development (R&D) for advanced technologies that contribute to national security needs.”²⁹

In DARPA’s view, warriors with superhuman physical capabilities are the wave of the future. In the words of a recent report by the agency to Congress, “DARPA’s approach is to imagine what a military commander

²²See An Act to authorize the Secretary of the Air Force to establish and develop certain installations for the national security, and to confer certain authority on the Secretary of Defense, and for other purposes, Pub. L. No. 85-325, § 7 (1958); see also U.S. Congress, Office of Technology Assessment, DEFENSE CONVERSION: REDIRECTING R&D, OTA-ITE-552, at 122 (Washington, D.C.: U.S. Government Printing Office, May 1993).

²³See DEFENSE CONVERSION at 122.

²⁴DARPA website, *DARPA Over the Years* [available at: www.darpa.mil/body/overtheyears.html].

²⁵See Dep’t of Def. Directive 5134.10, § 4, *Defense Advanced Research Projects Agency (DARPA)*, Feb. 17, 1995 (Certified Current as of Nov. 21, 2003); see also, Defense Advanced Research Projects Agency, *Strategic Plan*, 2-3 (Feb. 2003) [available at www.darpa.mil].

²⁶Dep’t of Def. Directive 5134.10, at § 3.

²⁷Dep’t of Def., Fiscal Year 2003 Budget Estimates, at D-25 (2002) [available at: <http://www.darpa.mil/body/pdf/FY03BudEst.pdf>].

²⁸See Dep’t of Def. Directive 5134.10 at § E1.1.1.13; see also DEFENSE CONVERSION, *supra* note 22, at 139.

²⁹DEFENSE CONVERSION at 121.

would want in the future, and then accelerate that future into being.”³⁰ As retired Rear. Adm. Stephen Baker, a former Navy chief of operational testing and evaluation, has declared, “[t]his “better warrior through chemistry” field is being looked at very closely.”³¹

Of the myriad ‘technical offices’ established under the DARPA umbrella to carry out the agency’s broad objectives, the Defense Sciences Office (DSO) is the division responsible for investigations into performance enhancement technologies:

The Defense Sciences Office mission is to vigorously pursue the most promising discoveries and innovations in science and engineering to create paradigm shifts in defense capabilities. DSO emphasizes programs in medical approaches to biological warfare defense, biology, materials and advanced mathematics.³²

In recent years, DSO has been focusing on the development of what it calls “Enhanced Human Performance” technologies “aimed at preventing humans from becoming the weakest link in the military.”³³ In addition to numerous technologies beyond the scope of this paper, DARPA has initiated a “Continuous Assisted Performance program” which “is investigating ways to prevent fatigue and enable soldiers to stay awake, alert, and effective for up to seven days straight without suffering any deleterious mental or physical effects and without using any of the current generation of stimulants.”³⁴ This initiative falls under the DSO objective to develop “medical approaches to . . . biology.” DARPA hopes that the fruits of this research will effect a complete change in the way America fights wars, providing a marked advantage in combating less technologically-advanced adversaries.³⁵ Further, while ‘go pill’ usage in recent years has likely been confined to aviators and, perhaps, special operations forces, DARPA believes that the tactical benefits of alertness are

³⁰See DARPA, *Strategic Plan* 2-3 (Feb. 2003).

³¹See Knickerbocker, *supra* note 16.

³³*DARPA Strategic Plan* at 18.

³⁴*Id.*

³⁵DARPA Defense Sciences Office, *Preventing Sleep Deprivation*. [available at: www.darpa.mil/dso/thrust/biosci/cap.htm] (“Eliminating the need for sleep during an operation, while maintaining the high level of both cognitive and physical performance of the individual, will create a fundamental change in warfighting and force employment. . . In short, the capability to operate effectively, without sleep, is no less than a 21st century revolution in military affairs that results in operational dominance across the whole range of potential U.S. military employments.”)

of such a general nature that “this advantage is not restricted by Service roles and missions.”³⁶ Therefore, it seems reasonable to conclude that any useful technologies that resulted from this initiative would likely find widespread use throughout the ranks.

Considering the secrecy of these projects and DARPA’s long-term approach to research, it is not surprising that the agency is somewhat vague about the specifics of their performance enhancement research: “[t]hese approaches will capitalize on emerging concepts in neuroscience, neurobiology, cognitive psychology, cell signaling/regulation, noninvasive imaging technologies, and novel mathematical approaches to modeling and analysis.”³⁷ Nevertheless, the details that DARPA has made public are sufficient to paint a somewhat frightening picture of the future of performance enhancement. Specifically, there are two general means of performance enhancement that DARPA seems to be exploring: powerful new psychoactive drugs and a medical device that would operate on the brain to ‘zap’ soldiers into alertness.

A. Traditional Pharmacological Approaches to Performance Enhancement

The most obvious way to move beyond “the current generation of stimulants” is to design a new generation of stimulants.³⁸ This is at least one objective of current DARPA research. Developing substances that can keep a soldier awake for up to seven days at a time, “would actually involve much more than the ‘linear, incremental and. . . limited’ approaches of stimulants like caffeine and amphetamines.”³⁹ Suffice it to say that

³⁶ *Id.*

³⁷ *Id.*

³⁸ See Knickerbocker, *supra* note 16.

³⁹ Knickerbocker, *supra* note 16.

it is likely that DARPA is investigating the possibilities of new compounds that would not be classifiable as amphetamines—or any other class of drugs currently available. Further, considering the far more pronounced effects on human physiology that DARPA hopes to achieve, it is not outside the realm of possibility that any such compound might have commensurately pronounced side effects.

B. Non-Pharmacological Approaches to Performance Enhancement

Apparently, at least some of the focus of DARPA research is focused on non-pharmacological medical devices, rather than drugs.⁴⁰ For example, Yaakov Stern, a neurologist at Columbia University who is being funded by DARPA, is attempting to develop an electromagnetic device that would “zap” soldiers into alertness.⁴¹ The idea of using any sort of ‘ray gun’ that would have a pronounced effect on the human brain should probably raise red flags about the potential for cancer, strokes, brain damage and cell mutation.

III. FDA’s Role in Regulating New Performance Enhancement Technologies

The regulatory concerns raised by DARPA’s current attempts to develop new means of military performance enhancement lie at an intersection between the two recent controversies over go-pills and experimental

⁴⁰ See 21 U.S.C. § 321(h) (“The term ‘device’...means an instrument...intended to affect the structure or any function of the body of man or other animals”); see also *United States v. 23... Articles*, 192 F.2d 308 (2d Cir. 1951) (holding that even a phonograph record intended to alleviate insomnia constitutes a medical device under § 321(h)).

⁴¹ Charles Laurence, *Ready for war in 2005: the soldier who never sleeps*, SUNDAY TELEGRAPH (LONDON) (Jan. 6, 2003) at 26.

protections against biological and chemical weapons. This section will examine the strategies that FDA has employed in the past to regulate food and drugs for military use. In addition, this section will demonstrate how the realities of an executive branch composed of agencies with disparate policy objectives and differing levels of political clout has complicated recent attempts by FDA to regulate potentially dangerous innovations that might, nevertheless, bolster our national security.⁴²

A.

The Historical Relationship Between FDA and the Military

Throughout the 20th Century, the relationship between FDA and the Department of Defense has been characterized by a conflict of institutional cultures, policy objectives and political clout:

An agency [FDA] designed to regulate a relatively decentralized part of the private sector found itself in competition (and often conflict) with much larger governmental agencies with radically different goals. Furthermore, the regulated industries sought to ally themselves with these competing governmental patrons and to resist FDA's control.⁴³

FDA's fight for regulatory control over food and drugs used in a military context has always been an uphill battle due to the basic characteristics of the agency: it is small, its Commissioner serves at the pleasure of the President rather than for a fixed term, the agency has always been subordinated under the umbrella of one or another Cabinet-level department, and it must continually combat a historical tendency to err on the side of national security, especially when the nation is at war.⁴⁴ FDA has only been successful in playing

⁴²My analysis of the 'go-pills' and bio-defense controversies builds upon three past papers in Prof. Barton Hutt's *Food and Drug Law* class at Harvard Law School. See Matthew A. Hoffman, *The Military's Need for "Speed": A Case Study On the FDA's Regulation of Off-Label Prescriptions* (2003) [available at: <http://leda.law.harvard.edu/leda/data/534/Hoffman.pdf>]; see also Christopher J. Lovrien, *Investigational Drug Use Among the Troops: The Waiver of Informed Consent in Cases of Military Combat Exigencies* (1997) [available at: <http://leda.law.harvard.edu/leda/data/164/clovrien.pdf>]; see also Brenda Jarrell, *FDA Regulation and the Military: Is There a Compromise in the Battle over Investigational Drugs?* (1997) [available at: http://leda.law.harvard.edu/leda/data/335/Brenda.Herschbach_Jarrell.pdf].

⁴⁴See *id.* at 456-59.

David to the Department of Defense’s Goliath due to its highly dedicated and capable staff, its success at maintaining “a high degree of credibility and respect,” and its secure position on the moral high ground as the protector of the general public against dangerous foods and drugs.⁴⁵

Interaction between FDA and the Department of Defense has been contentious due to the agencies’ conflicting policy goals. FDA maintains its administrative legitimacy because the regulation of food and drugs in the interest of protecting the public is “a classic and proper exercise of the police power” and implements Congress’ Constitutional mandate to regulate goods that travel in interstate commerce.⁴⁶ By contrast, the military derives its authority to win wars at all costs from an arguably more basic public policy interest in “provid[ing] for the common defense,” preserving the whole of American society when it is faced with a military threat to its very existence.⁴⁷

At the outbreak of the Second World War, Commissioner Campbell wrote that “the Food and Drug Administration can best serve the national emergency by redoubling our efforts to enforce the law, particularly as it applies to foods and drugs purchased and used by public agencies.”⁴⁸ This expression of FDA’s approach to regulation in wartime demonstrates the difficulty of positing a politically persuasive argument for the subordination of military efforts to FDA regulation. On one hand, Commissioner Campbell’s statement expresses a desire to protect America’s troops from dangerous foods and drugs by “redoubling” its enforcement efforts. On the other hand, however, conflict is inevitable where FDA focuses its regulatory microscope on the purchasing activities of other “public agencies.”

Many instances have arisen in which FDA enforcement would have served as a hindrance to military objec-

⁴⁵See *id.* at 456-61.

⁴⁶*Id.* at 462; see also *Hipolite Egg Company v. U.S.*, 220 U.S. 45 (1911); see also U.S. CONST. art. I. § 8, cl. 3.

⁴⁷See U.S. CONST. pmbl., art. I. § 8.

⁴⁸See Dean, *supra* note 43, at 470.

tives. Therefore, FDA has had to ‘choose its battles’ in the interest of maintaining its institutional legitimacy. During the Second World War, FDA engaged extensively in compromises with the military, conserving its regulatory powers for only those situations where the danger to the health of soldiers and/or civilians was most acute.

More often than not, FDA sought compromise, even when doing so ran contrary to the agency’s stated mission: “[o]n occasion FDA chose a tactical retreat to preserve their new alliances with the military services.”⁴⁹ For example, FDA relaxed filth standards for certain processed foods for the duration of the conflict as a concession to the realities of wartime strains on production.⁵⁰ And yet, those relaxations were never announced to the public.⁵¹ This policy of reticence regarding relaxed standards that could not be avoided could be interpreted as an attempt by FDA to preserve its political capital while yielding to interagency pressures to weaken, rather than “redouble,” its regulatory activities. On another occasion, FDA relaxed its labeling requirements for military packaging of an otic solution.⁵² FDA also agreed not to contest the military’s use of a then unapproved anti-malarial, quinine, so long as the dosage remained at a minimal level.⁵³ Similarly, FDA took a pragmatic approach to the difficult problem of setting standards for the production of penicillin. Faced with urgent wartime need for the nascent antibiotic, FDA relaxed its dating requirements for the drug so long as the Army took responsibility for developing adequate procedures for preserving the delicate new drug.⁵⁴

But, indeed, FDA did occasionally use its regulatory authority during the conflict to deny approval to the military—for example, regarding a nutrient-fortified candy bar proposed as a military ration—where the

⁴⁹*Id.* at 481

⁵⁰*See id.*

⁵¹*See id.*

⁵²*See id.*

⁵³*See id.* at 495-96 (“When faced with more than one scientific viewpoint and less wartime urgency, the policymaking process used for quinine likely would prove less successful.”).

⁵⁴*See id.* at 497-98.

argument could be made that approval would have made only a negligible contribution to winning the war.⁵⁵ In another example of FDA-military conflict, the War Department sought to be exempted from the FDCA's labeling requirements for all food products being supplied to the troops. While FDA "was in no position to force the military to follow the agency's advice," the agency succeeded in avoiding a blanket exemption, which it feared might compromise the civilian food supply, by entering into a dialogue with the War Department about its specific needs.⁵⁶

FDA's restrained approach in its relationship with the military proved to be a successful strategy, such that "[b]y war's end, FDA had won the confidence of the armed services." That confidence was built on a largely pragmatic approach to wartime regulation that has continued to prevail in recent years: while FDA does not always bend to the wishes of the military, it understands that the exigencies of the battlefield may make the stringency of peacetime regulation impractical and undesirable, except in the most severe instances of danger to soldiers. Therefore, FDA has continually worked with the military to fashion regulatory solutions that maintain the basic policy aims and authority of FDA without tying the hands of the Department of Defense.

On one hand, FDA's historical approach to regulation in the face of specific military needs seems almost inevitable. Without any guarantees that its directives will be followed by a military bent on achieving every possible advantage on the battlefield, FDA has been forced to compromise, contenting itself with the preservation of the outward appearance of its authority in instances where a conservative regulatory stance might simply be ignored by the armed services. However, while it is difficult to find fault with this overarching

⁵⁵See *id.* at 474.

⁵⁶See *id.* at 479-80.

system of interagency cooperation and compromise, we can still question the wisdom of FDA's actions in individual cases by conducting a cost/benefit analysis. To properly carry out its regulatory mission, FDA should only relax its standards in instances where the material benefit of an FDA concession to the war effort outweighs the attendant risks. Further, these risks could take multiple forms: risks to the health of the individual soldier, risks to the safety of those around him, and strategic risks to the war effort due to some unforeseen and debilitating side effect that an under-regulated food or drug might have.

For the most part, FDA decisions to under-regulate certain products during World War II were proven, in hindsight, to have been wise decisions. Penicillin was a godsend to military doctors treating battlefield wounds and likely saved innumerable lives and limbs. Similarly, it is likely that quinine did more good than harm for troops fighting in the insect-infested tropical climate of the southern Pacific Theater. However, when we apply this cost/benefit calculus to more recent concessions by FDA to the military during the Gulf War and in Afghanistan—in the context of 'go pills' and bio-defense drugs—that calculus does not necessarily come out in favor of under-regulation.

B. 'Go Pills'

During the 2002 military operations in Afghanistan, American aviators mistakenly attacked a Canadian unit in the field, killing four soldiers and injuring eight more.⁵⁷ Some critics argued that this tragic error in judgment was linked to the government-sanctioned practice of aviators taking amphetamines, an FDA-approved but controlled substance, in order to remain alert and awake during long sorties, which are often conducted at night. Although amphetamines are not experimental drugs, the manner in which they were

⁵⁷See Knickerbocker, *supra* note 16.

made available to American troops involved arguably inadequate practitioner safeguards for their off-label prescription. For example, according to NAVMED protocols, flight surgeons can “issue” stimulants, including Dexedrine, to pilots in “amounts required for one or two flights.”⁵⁸ However, the flight surgeon does not examine pilots before ‘prescribing’ the pills for a particular mission.⁵⁹ Instead, “ground testing” is done on a day prior to distribution of the pills—and that testing must occur on a day when no flying will actually take place.⁶⁰ The NAVMED guidelines are self-contradictory about what happens to unused pills after a mission is completed: although the flight surgeon is directed to “[c]ollect unused medication at the end of continuous operations[,]” he is also permitted to dispense enough ‘go pills’ for “two flights.”⁶¹ The careful but contradictory wording of these guidelines suggests an attempt to whitewash the realities of a process that looks far more like over-the-counter use than off-label prescription use.⁶²

In addition, the administration of amphetamines to soldiers raises a more general question about the ethics of using drugs for performance enhancement rather than for therapy. Just because our society has the ability to keep soldiers awake for days does not mean that we should exploit that capability. The military’s general approach to this criticism is to characterize ‘go pill’ usage as a therapy that is merely bringing tired pilots up to a baseline level of performance. This is evident in the terminology that the NAVMED guidelines employ, referring to “performance maintenance” rather than “performance enhancement.” However, the

⁵⁸See *NAVMED Guide for Flight Surgeons*, *supra* note 13, at 14.

⁵⁹See *id.*

⁶⁰See *id.*

⁶¹See *id.*

⁶²Section 353(b) of the Food, Drug and Cosmetic Act declares that “habit forming substances” as defined by §352(d)—which includes amphetamines—can only be administered with a written prescription. Because Dexedrine is only indicated for limited therapeutic purposes, including the treatment of narcolepsy and attention deficit disorder, prescription of this substance to prevent fatigue—the purpose for which the drug is being used in the military—is considered an off-label prescription. See *Prescribing Information for Dexedrine*, *supra* note 13, at 2. The intent of the prescription regime is to put adequate safeguards—the supervision of a qualified medical practitioner—on the use of dangerous drugs, while allowing doctors the flexibility to prescribe the drug on a case-by-case basis for reasons beyond the four corners of its approved indications. By reducing flight surgeon supervision to such a minimal level, the Navy and the rest of the armed services are trying to enjoy the benefits of off-label flexibility while flouting the safeguards of the prescription regime, which is meant to curtail unfettered use of potentially dangerous drugs.

truth of the matter is that the modern military services demand superhuman performance from airmen. The problem is that the logical conclusion to be drawn from this line of reasoning—that American aviators are being overworked, that perhaps we ask too much from our pilots—is incompatible with the perceived tactical requirements for mounting a successful military campaign. As was often the case during the Second World War, FDA has not stepped in to regulate the ‘go pill’ regime because to do so would likely put the military in an untenable position, basically forcing the Pentagon to ignore the regulatory authority of FDA, which would impair the future possibilities of coexistence between the two agencies.

C.

Drugs to Guard Against Chemical and Biological Attacks

During the 1990 Gulf War, American soldiers were forced to take experimental drugs—pyridostigmine bromide and botulinum toxoid—that had not yet been approved by FDA as the military sought to protect them from potential chemical and biological threats.⁶³ In recent years, it has been suggested that these experimental treatments may have contributed to Gulf War Syndrome.⁶⁴

Unlike Dexedrine, which has at least been approved by FDA and has therefore been subject to post-market surveillance for decades, the bio-defense drugs the military sought to dispense to combat forces were still investigational new drugs (IND). FDA takes very seriously the use of untested drugs on humans, as evidenced by its demanding, multiphase clinical trial system.⁶⁵ Therefore, because military objectives were

⁶³ See Alida Milner, *Gulf War Guinea Pigs: Is Informed Consent Optional During War?*, 13 J. CONTEMP. HEALTH L. & POL’Y 199, 223 (1996).

⁶⁴ See Robyn Pforr Ryan, *Should Combat Troops be Given the Option of Refusing Investigational Drug Treatment*, 52 FOOD DRUG L.J. 377, 378 (1997).

⁶⁵ See *The Food And Drug Administration’s Process for Approving New Drugs: Report of the Subcomm. on Science, Research and Technology of the House Comm. on Science and Technology*, 96th Cong. (1980) in Peter Barton Hutt and Richard A. Merrill, FOOD AND DRUG LAW: CASES AND MATERIALS 514-516 (1991).

incompatible with the parameters of the IND regime, FDA had to take action in order to preserve, at least ostensibly, the integrity of the entire regulatory framework. Section 355 of the *Food, Drug, and Cosmetic Act* sets out an extensive and stringent application procedure for INDs: “[n]o person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application. . . is effective with respect to such drug.”⁶⁶ However, in certain instances, the potential benefits of immediate access to a particular IND may greatly outweigh the attendant risks of pre-approval use. In such instances, FDA has allowed an exemption from these requirements, when the investigation is conducted by “experts qualified by scientific training and experience” and the experts obtain ‘informed consent’ from their subjects.⁶⁷

In requesting an exemption for the administration of these two bio-defense agents, the Department of Defense asserted that “special military exigencies sometimes must supersede normal rights and procedures that apply in the civilian community.”⁶⁸ In response, FDA crafted a regulation allowing an exception to the informed consent requirement in the rare instance where obtaining informed consent was “not feasible.”⁶⁹ Subsequently, FDA Commissioner Kessler waived the informed consent requirement for the bio-defense vaccination program pursuant to the new non-feasibility exception.⁷⁰

This act by FDA is in line with its generally conciliatory approach in dealing with the military since the Second World War. However, the possibility that the administration of these experimental drugs contributed to gulf war syndrome suggests that this is an instance where the case-specific cost/benefit calculus might have been wrong. American military personnel were not subject to chemical or biological attacks during the

⁶⁶21 U.S.C. § 355(a).

⁶⁷21 U.S.C. § 355(i)(1), (3).

⁶⁸See Milner, *supra* note 61, at 224 (quoting letter from the Assistant Sec. of Def. (Health Affairs) to the Assistant Sec. of Health for HHS).

⁶⁹See 21 C.F.R. 50.23(a) (1995); *see also* Milner, *supra* note 61, at 226 n 186.

⁷⁰See Milner at 226.

Gulf War. Therefore, at least in hindsight, there was no real military risk to speak of. However, we are now seeing that there may have been an enormous health risk to the individual soldiers who were forced to take the experimental drugs.

IV. FDA Regulation and the Next Generation of Military Performance Enhancement Technologies

In general, recent scholarship on the relationship between FDA and the military has focused on either ‘go pills’ or the experimental vaccine regime, but has not considered both controversies in conjunction.⁷¹ Because current DARPA research into new experimental techniques for performance enhancement implicates regulatory and policy concerns raised by both controversies, it is useful to take a new, hybrid approach when examining this potential area of FDA/military interaction.

DARPA has made it clear that they are experimenting with anti-fatigue technologies—both drugs and medical devices—that heretofore have not been approved by FDA, and it is not outside the realm of possibility that the Pentagon might some day ask FDA for an exemption allowing for their pre-approval use in combat. While the practical application of these technologies would be the same as for ‘go pills,’ they would still be experimental. Therefore, the regulatory concerns are slightly different from those that have arisen in the context of ‘go pills.’ These hypothetical compounds would not be prescribed off-label. Rather, the experimental technologies would more closely resemble the experimental vaccines and bio-defense INDs that received an exemption from FDA during the Gulf War.

⁷¹For a study of the policy and regulatory implications of the “go pills” controversy, see Hoffman, *supra* note 41. For scholarship on the informed consent requirement as it relates to the mandatory use in the military of experimental bio-defense drugs, see Lovrien, *supra* note 41; see also Alida Milner, *Gulf War Guinea Pigs: Is Informed Consent Optional During War?*, 13 J. CONTEMP. HEALTH L. & POL’Y 199 (1996); see also Suzanne B. Seftel, *Justiciability: Waiving for the Flag: Should Informed Consent Rules Apply in the Context of Military Emergencies?*, 60 GEO. WASH. L. REV. 1387 (1992); see also Ryan, *supra* note 62; see also Natasha Tidwell, *Soldiers of Misfortune: The Justiciability of Injunctive Relief Actions in the Federal Courts and the U.S. Military’s Mandatory Anthrax Inoculation Program*, 37 NEW. ENG. L. REV. 429 (2003).

At the same time, because these technologies are intended to effect performance enhancement rather than to protect against the threat of biological and chemical attacks, the informed consent issue becomes far murkier than it was regarding experimental vaccines before the Gulf War. First, the Pentagon could argue that there is no need for a waiver of informed consent because ingesting ‘go pills’ is entirely voluntary. However, the realities of the ‘go pill’ procedure are such that aviators already feel a strong institutional pressure to take the pills: sorties have become so long and frequent that the job makes superhuman demands on pilots. Military personnel who refuse to take ‘go pills’ might be incapable of achieving an adequate level of performance, endangering their fellow soldiers and themselves, and likely running the risk of being grounded by their commanding officers. Therefore, FDA could certainly argue that a waiver of informed consent would be required.

However, the new generation of ‘go pills’ and ‘go devices’ would change the ‘combat exigency’ calculus. FDA would have greater difficulty justifying such a waiver because fatigue borne of an overly grueling combat schedule is not as persuasive a combat exigency as the risk of chemical attacks was before the Gulf War. These are not technologies intended to protect American troops from some horrifying weapon that our enemies might use in a combat situation. Instead, these are technologies intended to enhance performance. While it might be argued that American soldiers will be at greater risk of death in combat without these new technologies, this is a far weaker policy argument for an exemption than that posited in preparation for the Gulf War.

Based on the pattern of past interactions between FDA and the military, it is reasonable to conclude that FDA would find some way to justify any exemption from IND requirements that the Pentagon might request for the next generation of experimental performance enhancement technologies. The Gulf War vaccination

program demonstrates that the Pentagon seems intent on giving its troops every tactical advantage while they are in combat, even if those advantages are distinctly disadvantageous to the long-term health of American servicemen. However, whatever FDA regulators privately think about the ‘supersoldier’ of the future, any attempt to materially change military policy would likely result in the Pentagon simply flouting FDA regulatory control. FDA would have only one recourse in order to fulfill its philosophical stance that “[t]he people who are in the armed forces are entitled to the protection which they ordinarily enjoy as citizens.”⁷² In a word: publicity. FDA has an incredibly powerful reserve of moral authority, which it could leverage by making noisy protestations in the news media about the reckless Pentagon’s plans to endanger the lives of the men and women who work daily to secure freedom for all Americans. The elected officials—the president and Congress—who oversee the activities of the Department of Defense might take heed and apply pressure internally on Pentagon officials to take a more conservative approach and curtail their aspirations to create a ‘supersoldier.’

Conclusion

DARPA’s performance enhancement initiative is only one example of the Pentagon’s growing interest in finding military applications for experimental drugs and medical devices.⁷³ Advances in drug development and biotechnology suggest that, in the future, the Department of Defense will have an even wider array of technologies to choose from, placing increasingly greater demands on FDA’s regulatory apparatus. While FDA’s publicity capabilities are formidable, they are not a conclusive solution to the growing problem of

⁷²Dean, *supra* note 43, at 480 (quoting Letter from J.C. Clark, Chief, Cent. Dist., FDA, to Chiefs, Cent. Dist. Stations, FDA (Mar. 11, 1942) (F: 040.2 Cooperation With Other Agencies, Gen. Subject Files, 1945, RG 88, NARA-CP)).

⁷³See George J. Annas, *Protecting Soldiers from Friendly Fire: The Consent Requirement for Using Investigational Drugs and Vaccines in Combat*, 24 AM. J. L. AND MED. 245, 258 (1997) (The U.S. military is interested in the possible combat-related use of approximately twenty vaccines which are currently investigational.) (citing Joint Program Office for Biological Defense, U.S. Dep’t of Army, Joint Vaccine Acquisition Program: Final Programmatic Environmental Assessment (June 1997)).

systematic regulatory deference to the military's desire for unfettered access to experimental technologies. As Viking rulers learned a millennium ago, the use of performance enhancing drugs in combat can be a double-edged sword. Today, officials at all levels of the federal government—administrators, legislators, the President, and his cabinet—need to take an honest look at the potential risks and rewards of current initiatives in military pharmacology and develop the regulatory tools that will guide our military performance enhancement policy in the future, for the good of all Americans, whether or not they wear a uniform.